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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/956,004	09/20/2001	Patrick J. Dillon	PB324D1	1504

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EXAMINER
LY, CHEYNE D

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 01/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/956,004	Applicant(s) DILLON ET AL.	
	Examiner Cheyne D Ly	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-66* is/are pending in the application.

4a) Of the above claim(s) *64-66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *34-66* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Search Result 4* .

DETAILED ACTION

1. Applicant's election with traversal of Group I, claims 34-63, in Paper No.5, filed October 18, 2002, is acknowledged.

2. The traversal is on the ground(s) that it would not be unduly burdensome to perform a search on claims 1-33 together. This is not found persuasive because the inventions of claims 1-33, which have been restricted to Groups I-X, Paper No. 3, are distinct inventions due to the different chemical types or methods regarding the critical limitations therein. Applicant argues that "the searches for polynucleotides, polypeptides, antibodies, and methods of making and using the same commonly overlap, the search and examination of Groups I-X would not entail a serious burden." It should be noted that these inventions in addition to being distinct as defined above; they are also are related as product and process of use. The inventions can further be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). While taking advantage of the distinct properties of each chemical type, these usages have distinct goals as requiring distinct and different functions and results thereof without overlapping search due to different subject matter. This lack of overlapping searches documents the undue search burden if they were search together.

3. The requirement is still deemed proper and is therefore made FINAL.

4. Claims 64-66 are withdrawn from examination because these claims are directed to a method for detecting Escherichia coli as oppose to an isolated nucleic acid molecule and a

method for making a recombinant vector comprising of said nucleic acid molecule (See Page 2, Group I, Paper No. 3, mailed August 21, 2002).

5. Claims 34-63 are examined on the merits.

LACK OF UTILITY UNDER 35 U.S.C. § 101

6. The pending claims have been reviewed in light of the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first paragraph, "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001.

7. The examiner is using the following definitions in evaluating the claims for utility.

"Specific" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure that is probative of the applicant's assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

8. Claims 34-63 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility.

9. The claimed subject matter is not supported by a specific, substantial, and credible utility because the disclosed uses are generally applicable to broad classes of this subject matter. In addition, further characterization of the claimed subject matter would be required to identify or reasonably confirm a "real world" use. The examiner does not find an adequate nexus between the disclosure of record and the asserted properties of the claimed subject matter.

10. The critical limitation of claims 34-63 is an isolated polynucleotide SEQ ID NO: 65 represented by nucleotides 2889-1915. While some data are supplied indicate that SEQ ID NO: 65 and thereof were sequenced through a "high through-put sequencing of clones covering PAI IV and PAI V in E. Coli J96" (Page 35, Lines 35 to 37). Open reading frames (ORF) were identified using GeneMark based on second-order Markov model trained from known E. coli coding regions and known E. coli non-coding regions. The important genes that are implicated in the virulence of E. coli J96 PAIs are adhesions, excretion pathway proteins, proteins that participate in alterations of the O-antigen in the PAIs, cytotoxins, and two-component (membrane/DNA binding) proteins (Pags 36-7, Paragraph 0154). Each ORF and its corresponding nucleic acid sequence was assigned to the gene function mentioned above based on its similarities to protein from an organism listed in Tables 1-3 (Page 9, Paragraphs 0046-0048).

11. However, the disclosure of the similarity of a particular sequence to another by sequence comparison without specific and substantial disclosure as to the specific identity and function of

a nucleotide composition as defined by specific and substantial biological activity does not support the claimed asserted utility of the said composition. It is noted that applicant has identified a sequence which is known in the prior art and which has a stated sequence similarity to the claimed sequence. Absent factual biological activity data, one skilled in the art would have reason to doubt that sequence similarity alone would reasonably support the assertion that the biological activity of the claimed subject matter would be the same as that of the similar sequence. Furthermore, it is unclear whether the similar sequence identified in the prior art has actually been tested for the biological activity or whether this also is an asserted biological activity based upon sequence similarity to yet a different sequence.

12. Note that it would have been well known in the art that sequence similarity does not reliably correlate to structural similarity and that structural similarity does not reliably result in similar or identical biological activities. For example, it would have been well known that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. In the absence of factual biological activity data characterizing the structural and functional components of the biomolecule, the effects of these changes are largely unpredictable as to which ones will have a significant effect and which ones will be silent mutations having no effect. Several publications document the unpredictability of the relationship between sequence, structure, and function, although it is acknowledged that certain specific sequences have been found to be conserved in biomolecules having related function following a significant amount of further research. See Lopez et al. (Molecular Biology, 32:881-891,1999); Attwood (Science, 290:471-473, 2000); Gerhold et al. (BioEssays, 18(12):973-981, 1996); Wells et al. (Journal of Leukocyte Biology, 61(5):545-550, 1997); and

Russell et al. (Journal of Molecular Biology, 244:332-350, 1994). However, this level of factual biological activity data is absent here.

CLAIMS REJECTED UNDER U.S.C. § 112, FIRST PARAGRAPH

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

LACK OF ENABLEMENT

14. Claims 34-63 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the claimed sequence. For a sequence putatively assigned a biological function, even if correct, does not appear to be defined as to what use it is to be applied to. The significance of the sequence is undefined, further rendering it indiscernible how someone of skill in the art would use such an entity.

15. Due to the large quantity of experimentation necessary to determine activity or property of the disclosed nucleic acid such that it can be determined how to use the claimed sequence, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, and the breadth of the claims which fail to recite particular biological activities, the specification fails to teach the skilled artisan how to make and use the claimed invention.

16. Also, since the claimed invention is not supported by a specific, substantial, and credible utility or a well-established utility for the reasons set forth above (refer to 35 U.S.C. § 101 rejection), one skilled in the art would not know how to use the claimed invention.

NEW MATTER REJECTION

17. Claims 35, 36, 40, and 42-63 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Each of the specific rejections below is A NEW MATTER REJECTION.

18. Specific to the body of Claims 35, 36, 44, 45, 53 and 54 the introduction of "heterologous polynucleotide sequence" is considered to be NEW MATTER. It is acknowledged that Applicant discloses "heterologous ORF" in Paragraph 0068, Line 7, but not "heterologous polynucleotide sequence."

19. Specific to the body of Claims 40, 42, 49, 51, 58, and 60 the introduction of "polynucleotide is operably associated" is considered to be NEW MATTER.

20. Specific to the body of Claim 43 the introduction of hybridization conditions that comprise of "at 50-65°C", "0.5XSSC at 50-65°C" are considered to be NEW MATTER. It is acknowledged that Applicant discloses hybridization conditions that are "incubation at 42°C" and wash with 0.1XSSC at 65°C (Page 13, Paragraph 0058). Claims 44-51 are rejected for being dependent from Claim 43.

21. Specific to Claim 52, Line 2, the introduction of "at least 15 contguous nucleotides" is considered to be NEW MATTER. It is acknowledged that Applicant discloses the limitation of

fragments of "at least about 15 nucleotides" (Page 12, Paragraph 0056, Line 4). Claims 53-63 are rejected for being dependent from Claim 52.

22. Specific to Claim 61, Line 2, the introduction of "at least 20 contiguous nucleotides" is considered to be NEW MATTER. It is acknowledged that Applicant discloses the limitation "at least about 20 nucleotides" (Page 12, Paragraph 0056, Line 4).

23. Specific to Claim 62, Line 2, the introduction of "at least 40 contiguous nucleotides" is considered to be NEW MATTER. It is acknowledged that Applicant discloses the limitation of fragments of "at least about 40 nucleotides" (Page 12, Paragraph 0056, Line 5).

24. Specific to Claim 63, Line 2, the introduction of "at least 500 contiguous nucleotides" is considered to be NEW MATTER. It is acknowledged that Applicant discloses the limitation of fragments of "larger fragments 50-500" nucleotides (Page 12, Paragraph 0056, Line 6).

CLAIMS REJECTED UNDER U.S.C. § 112, SECOND PARAGRAPH

25. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

26. Claims 38, 40, 42, 43, 47, 49, 51, 56, 58, and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

27. Specific to the body of Claims 40, 42, 49, 51, 58, and 60, the phrase "operably associated" is vague and indefinite. It is unclear which criteria the applicants regard as "operably associated" (i.e. adjacent or binding nucleotide sequence). Applicants can resolve this issue by particularly pointing out the criteria that is used to determine that a polynucleotide that is "operably associated." Clarification of the metes and bounds of the instant claims is required.

28. Specific to Line 1 of Claims 38, 47, 56; and Line 4 of Claim 43, the phrases "sequence complementary" and "complementary strand" are vague and indefinite. It is unclear which criteria the applicants regard as complementary. Does a complement of 2 nucleotides sufficient to consider such polynucleotide complementary? Applicants can resolve this issue by particularly pointing out the criteria that is used to determine that a sequence is "complementary". Clarification of the metes and bounds of the instant claims is required.

Claim Rejections - 35 USC § 102

29. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

30. Claims 38, 43-51 and 56 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Valenuela et al. (US PN 5,814,478).

31. Valenuela et al. (US PN 5,814,478) teaches an isolated nucleic acid molecule set forth in SEQ ID NO:31 comprising a nucleotide sequence encoding a polypeptide having the MuSK-activating activity of human agrin (Claim 1). An expression vector comprising a nucleic acid molecule of claim 1, 2, 3 or 4 wherein the nucleic acid molecule is operatively linked to an expression control sequence (Claim 10). A host-vector system for the production of a polypeptide having the MuSK-activating activity of human agrin which comprises the vector of claim 10, in a suitable host cell (Claim 11). Consistent with the scope of claims 38, 43-51 and 56

the fragment of SEQ ID NO:31 representing nucleotides 457-463 of Valenuela et al. is complementary to the fragment representing nucleotides 2459-2465 (CCAGTCA) of SEQ ID NO:65 of this instant case.

CONCLUSION

32. NO CLAIM IS ALLOWED.

33. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 193), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

34. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (703) 308-3880. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

35. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

36. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

C. Dune Ly
12/24/02

ARDIN H. MARSCHEL
PRIMARY EXAMINER